REMARKS

Claims 1-5, 7-30, 38 and 53-56 are pending. Claims 6, 31-37 and 39-52 have been canceled without prejudice. The amendments to the independent claims recite terms and concepts previously found in dependant claims. As such, no new matter or new issues are present. Support for the amendments is found throughout the specification, for example on page 1, second sentence under "Field of the Invention". Reconsideration of the rejection is respectfully requested.

Claims 3 and 4 were rejected under 35 USC 112, first paragraph as failing the written description requirement. A through discussion of the inadequacies of this rejection was discussed previously in the response filed July 7, 2003. The examiner raises another issue alleging a "core structure" for the IRES is not disclosed and the structure function relationship for the IRES is missing. This rejection is respectfully traversed.

As stated in the specification on pages 23-24, a wide variety of different structures function as an IRES. Even reversing the orientation of the IRES maintains its function. This assertion is supported by the prior art of record, specifically Ivanov et al, page 41, figure 9 and page 42, column 1, lines 21-24 and column 2, lines 2-6. The examiner's requirement for naming a "core structure" is unreasonable for the present invention as many structures function in the same manner and the structures lack a specific "core structure". Likewise for the "structure-function relationship" which the examiner alleges to be missing. The term IRES is primarily a functional description of a nucleic acid sequence, which is adequately described in the specification as filed.

The specification discusses the chemical structure of the IRES using only the broadest of definitions, namely that it is a polynucleotide sequence (a polymer of ribose or deoxyribose coupled by phophodiester linkages where the ribose or deoxyribose is derivatized by one of four different bases). Should one consider this a "core structure" it is clearly within the written description of the specification. Accordingly, this rejection should be withdrawn.

Claims 6-8, 12-17 and 19-29 were rejected under 35 USC 103 as being unpatentable over Santa Cruz et al in view of Ivanov et al for reasons of record. Claim 6

was canceled in the amendment filed June 26, 2003 and need not be further considered. The comments given in the final rejection mailed October 6, 2003 mischaracterize applicants arguments, specifically appellants wish to emphasize the lack of motivation to create the claimed invention, not that any alleged increase in expression is adequate motivation. Applicants argue that no expression at all was expected, not a quantitative difference. Santa Cruz et al expresses a fusion protein was produced from one translation event that is quite different from the present invention with separate expression of two proteins from two separate translation events. Ivanov et al doesn't even express a viral vector. Thus, the examiner lacks motivation to expect expression from her unsuggested taking of parts of these two references to meet the claimed invention.

Furthermore, all of the claims have been amended to recite that the IRES sequence is heterologous from the viral vector and/or the protein whose expression is controlled by the IRES. Note page 7, fourth paragraph of the specification as to the requirements of "heterologous". Santa Cruz et al does not mention using an IRES at all and suggests nothing as to its use. Ivanov et al always uses an IRES that is homologous to both the vector and the viral coat protein under its control. Ivanov et al emphasizes in several locations that different viruses have very different IRES sequences and that an IRES from one virus will not function in a different virus, even when they are closely related. Therefore, Ivanov et al cannot suggest, cannot motivate and also specifically teaches away from using their IRES in any heterologous viral vector system.

Support for these assertions are found in Ivanov et al in multiple locations.

1.) the abstract, lines 11-13: "*The capacity of crTMV IREScp for mediating internal translation distinguishes this CP tobamovirus from the well-know-type member of the genus, TMV U1.*"

2.) page 40, second column, lines 2-5: "*Unexpectedly, our experiments have shown that, unlike TMV U1 RNA, genomic RNA of crTMV tobamovirus directs synthesis of CP in vitro (Fig. 1A).*"

3.) page 41, second column, lines 4-10: "*In order to demonstrate that IREScp-mediated translation is unusual for tobamoviruses, ... Figures 7B and 7C*

show that TMV U1-derived sequence was incapable of mediating internal ribosome entry."

Given the similarities between the viruses crTMV and TMV and the Ivanov et al teaching that the IRES of TMV is "incapable" of functioning in crTMV, it would be unobvious to consider an IRES capable of functioning in a heterologous vector as applicants have claimed and demonstrated in their specification examples.

Furthermore, IRES sequences are very different in different virus species as mentioned in several locations.

4.) Figure 9 compares the IRES directing translation of the coat protein gene(s) from 11 different tobamoviruses. Note the very wide divergence between certain different sequences.

5.) Page 42, first column, lines 21-24: *"Our results indicate that the structure of IREScp, which is relatively short and simple (Fig. 6), is markedly distinct from IRESes of picornaviruses and other eukaryotic mRNAs described so far."*

6.) Page 42, second column, lines 2-6: *"the nucleotide sequence comparison of 150-nt region upstream of CP genes shows that this region is highly conservative between crucifer-infecting tobamoviruses and is strongly different from other tobamoviruses (Fig. 9)."*

Such large differences in sequences between different IRESes further indicates the lack of motivation to use an IRES in a heterologous system. This is particularly true when in at least one example, the IRES from one virus was not functional when inserted in a different viral vector system. (quote #3 above)

Applicants wish to emphasize that the concept of using an IRES with a heterologous system, was present in previously pending dependant claims. Presently all of the claims have been amended or inherently claim this recitation. Accordingly, the rejection should be withdrawn.

Claims 1-3, 5, 9-11, 18, 30 and 53-56 were rejected under 35 USC 103(a) as being unpatentable over Ivanov et al in view of Santa Cruz et al. This rejection is essentially the same as above, applied to additional claims. These claims were also amended to recite that the IRES is heterologous to the viral vector and/or viral protein.

The examiner stated, "Absent evidence to the contrary, one of ordinary skill of art would have reasonable expectation of success..." As shown above, applicants have pointed out evidence in the Ivanov et al reference showing that a construct was made with an IRES heterologous to the viral construct and that the IRES was not functional in that heterologous viral construct.

Of course, in the specification, an IRES heterologous to the viral construct is functional but the construct is a viral vector (as claimed) and its function results in *in vivo* expression (in the specification) as opposed to *in vitro* translation (in Ivanov et al).

For all of the reasons given above in the previous 103 rejection given above, this rejection over the same references should likewise be withdrawn.

CONCLUSIONS

In view of the amendments and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance are respectfully requested. If any issues remain, the examiner is encouraged to telephone the undersigned.

If needed, applicants petition for an extension of time under the provisions of 37 CFR 1.136(a) for sufficient time to accept this response. The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,

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enclosures: (1) NOTICE OF APPEAL
(2) PETITION FOR 1 MONTH EXTENSION OF TIME.